

Cofactor strap regulates oxidative phosphorylation and mitochondrial p53 activity through ATP synthase

ABSTRACT

Metabolic reprogramming is a hallmark of cancer cells. Strap (stress-responsive activator of p300) is a novel TPR motif OB-fold protein that contributes to p53 transcriptional activation. We show here that, in addition to its established transcriptional role, Strap is localised at mitochondria where one of its key interaction partners is ATP synthase. Significantly, the interaction between Strap and ATP synthase downregulates mitochondrial ATP production. Under glucose-limiting conditions, cancer cells are sensitised by mitochondrial Strap to apoptosis, which is rescued by supplementing cells with an extracellular source of ATP. Furthermore, Strap augments the apoptotic effects of mitochondrial p53. These findings define Strap as a dual regulator of cellular reprogramming: first as a nuclear transcription cofactor and second in the direct regulation of mitochondrial respiration.

Keyword: Cofactor strap; Oxidative phosphorylation; Mitochondrial p53; ATP synthase